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Poisonous medicinal plants used in the popular pharmacopoeia of the Rif, northern Morocco

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ABSTRACT

Popular herbal medicine has served as a unique health provider for human beings for thousands of years. In the present study, we document the toxic plants used as medicines in the Rif, intending to assess the knowledge of indigenous people on the toxicity of the natural products used. Ethnobotanical survey was conducted in the Rif, northern Morocco between June 2016 and June 2018 using semi-structured questionnaires and focus groups. An investigation of the scientific literature was conducted to sustain or verify the claimed toxicological information. A total of 84 species of plants belonging to 67 genera and 30 families were reported as being used in the prevention and treatment of diseases. The families reported to be most representatives of these kinds of plants are Asteraceae and Fabaceae (7 species). However, the highly toxic plant prescribed was *Rosmarinus officinalis* L. Leaf was the most commonly used plant part, and the majority of herbal remedies were prepared from a decoction (40.6%). The results of this investigation showed that the local people in the Rif are still dependent on herbal medicine. These species used for remedial purposes are noted to have a potential toxic impact associated with their irrational consumption. Therefore, we recommend that attention should be observed when using them as medicinal sources.

1. Introduction

The history of herbal medicine, from ancient times to the present day, is rich in teachings. Since its appearance, only 3 million years ago, humans have used fine plants as food (Erwin, 2015). Whether the plant is edible or toxic, it is used to kill the game and the enemy or to heal, humans have discovered through a series of failures and successes, the use of plants for his well-being (Tabuti et al., 2003). At present, herbal medicines can help us provide interesting solutions to the constraints associated with health, especially in developing countries. In the Moroccan Rif, phytotherapy is an ancient practice, which owes greatly to Arabo-Amazigh medicine, even if non-Muslims, Jews, and Christian particularly, have played an important part in this regard.

Like all synthetic medicines, the use of medicinal plants causes deleterious effects on the human and animal body. The preponderance of medicinal plants contains dozens of complex composites, some of them with high complexity. Really, of about 400 000 plants studied, most of them comprise toxic substances (Ishii et al., 1984). This said it resembles that medicinal plants should be used with precautions and toxicology investigations conducted to improve the knowledge of the plant or plant preparation given to communities (Mounanga et al., 2015). It has been shown that the toxicity of a given medicinal plant species depends on different factors (Bellakhdar, 1997a; Bruneton, 1996a), including the dose used, the strength of secondary metabolites, the harvest season, the time of exposure, the climate and soil, the preparation mode (infusion, maceration, decoction, raw and cooked), the part used (root, fruit, leaf, stem, seed, and bark).

Cases of intoxications reported by the Center Antipoison and Pharmacovigilance of Morocco (CAPM) show that health problems due to irrational, anarchic, and uncontrolled practices of plants are far from negligible. In Morocco, plants were responsible for 5.1% of intoxications announced in the period between 1980 and 2008. The toxicity of plants usually produces morbidity and mortality. During the period registered, there were 4287 cases of poisoning, of which 357 cases were recorded as the maximum value in 2003. The high number of deaths was reported in 10 cases in 2001 (Rhalem et al., 2009a).

Abbreviations: DD, Dermatological Diseases; DSD, Digestive system diseases; GUD, Genito-Urinary diseases; MD, Metabolic Diseases; ND, Neurological Diseases; RD, Respiratory Diseases; FC, Frequency; RFC, Relative Frequency of Citation; PPV, Plant Part Value; ICF, Informant Consensus Factor.

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Knowledge of the toxicity of the Moroccan plant species is only available to a low degree Due to the absence of ethnopharmacological and toxicological studies in this area. We have little evidence that the risks of herbal medicine are clinically significant; this is explained by the lack of research in this field. It has recently reported that only 15% of randomized clinical studies of the evaluation of medicinal plants have taken into account the side and toxic effects of these plants (Zekkour, 2008a). The main aim of this study is the valorization of poisonous medicinal plants and to provide an overview on the state of plant biodiversity of toxic medicinal plants, recommended by the actors of traditional medicine (herbalists, elder people, traditional healers, and druggists) in this region.

2. Materials and methods

2.1. Study area

The present study was carried out in the Rif (North of Morocco). It is bounded in the North by the Strait of Gibraltar and the Mediterranean Sea, in the South by the Rabat-Sale-Kenitra region and Fez-Meknes region, in the West by the Eastern Region, and in the West by the Atlantic Ocean, with the geographical coordinates between 34° and 36° of latitude in the North and −4° to −6° of longitude in the West (Fig. 1). The total geographical area of the Rif is 11 570 km^2 and urban population is about 3 549 512 inhabitants (HCP, 2018). The society is mixed between Imazighen and Arabic ethnicity.

The study area is distinguished by a Mediterranean climate with a maximum temperature beyond 45 °C during summer (July–August) and below 0 °C during winter (December–January) and the average annual precipitation ranges from 700 to 1300 mm which falls largely between October and February (DMNM, 2018). It is a mountainous with altitudes ranging from 145 to 2456 (Jbel Tidirhine) m a.s.l. Principally inhabitants of Rif are very greatly reliant on the subsistence agriculture, livestock, and to a minor extent, from forest reserves for their livelihood.

2.2. Methodology

2.2.1. Ethnobotanical survey

The ethnobotanical study was carried out from June 2016 to June 2018 to collect knowledge on toxic plants used in the popular local pharmacopoeia of the Rif following standard method (Cotton, 1996; Martin, 2014). The techniques applied for data gathering were semi-structured conversations (Klotoé et al., 2013), focus group discussions, and noted and recorded with a digital voice recorder. 1000 informants within aged 18–86 years were randomly chosen for interviews (elder people, bonesetters, herbalists, and therapists) in the Rif. By conducting a stratified random sampling, samples are then formed in each of the 28 strata, including seven urban communes: [S1: Al Hoceim (40), S12: Chefchaouen (40), S15: Tétouan (40), S19: Martil (40), S20: Md'q (40), S21: Fnideq (40), S26: Tanger (41)] and twenty-one rural communes: [S2: Ajdir (35), S3: Izefzafen (30), S4: Bni Hadifa (30), S5: Targuist (40), S6: Tizi n Tchin (30), S7: Issaguen (34), S8: Bab Berred (35), S9: Cherrafate (30), S10: Bab Taza (30), S11: Derdara (29), S13: Akchour (35), S14: Fifi (30), S16: Bni Karrich (40), S17: Mallalyène (35), S18: Zinat (36), S22: Belyounich (35), S23: Melloussa (39), S24: Ksar Esghir (34), S25: Bni Ouassin (36), S27: Al Bahraouiyne (39), S28: Jouamaa (39)] and they are put together to make up the overall sample of 1000 informants. Knowing that the number of people surveyed varies from one stratum to another depending on the abundance of medicinal plants sought. The information collected concerned the demographic characteristics (age, gender, level of study, family situation, and source of knowledge about toxic species), and the ethnobotanical data for each plant includes the common local name, the route of administration, the method of preparation, the part used, and the diseases treated (Appendix A). The inhabitants in the study area speak Amazigh, Arabic dialects and therefore, informants were conducted in Amazigh or Arabic dialects. All the documented data was later translated into English.

2.2.2. Toxic species collection, identification, and deposition in herbarium

Based on ethnobotanical data provided by our respondents, plant species with their correct local nomenclature were organized alphabetically by family name, and illnesses treated. The identification of the collected toxic plants was done first in the field and completed at the

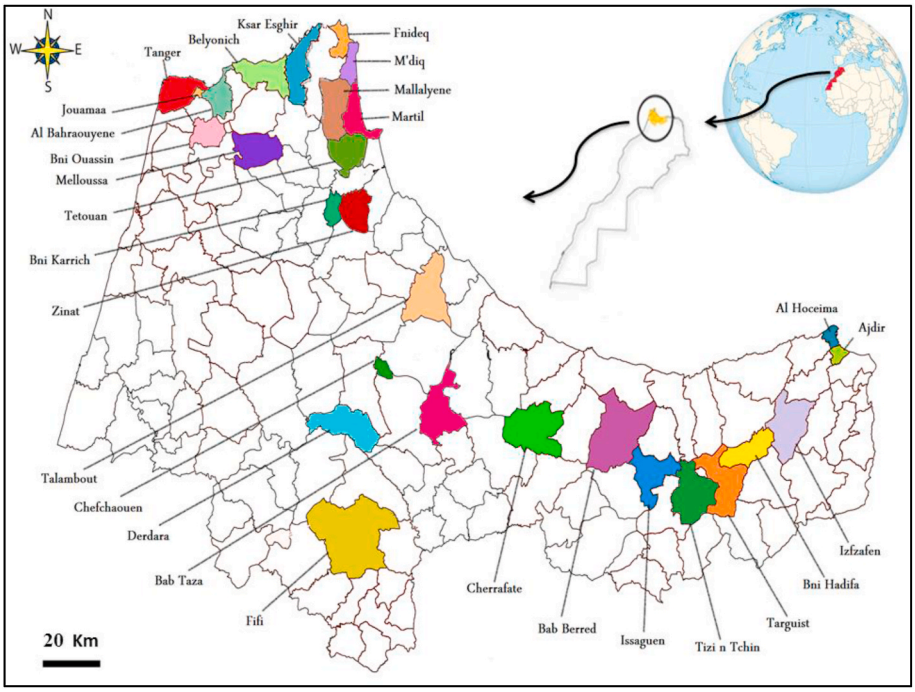

Fig. 1. Geographical location of the study area.

Nutrition, Health, and Environment Laboratory. These toxic plants mentioned by the informants have taxonomically identified thanks to the documents: Toxicology in Morocco (Charnot and Faure, 1945), Aggressive plants and plant poisons (Delaveau, 1974), Effects of poisonous plants on livestock (Keeler et al., 1978a; 2013b), "Toxic plants - plants dangerous to humans and animals" (Bruneton, 1996b), "Traditional Moroccan pharmacopoeia, ancient Arab medicine and popular knowledge" (Bellakhdar, 1997b), and "The risks of herbal medicine, monographs of the most common toxic plants in Morocco" (Zekkour, 2008b). In order to check the state of plants compiled from literature research and to update the name of plant species, in accordance with International Plant Names Index and "Angiosperm Phylogeny Group III" 2009 (APG III), we used the following databases: "The plant list 2009"(http://www.theplantlist.org) and "African Plant Database 2016"(https://www.ville-ge.ch/musinfo/bd/cjb/africa/recherche.php). Only the names of plants accepted by one of these databases were retained to be listed in this paper. All voucher specimens have been preserved, stored, and archived in the Ibn Tofail University, Morocco Herbarium for future reference.

2.2.3. Statistical analysis

Data collected during this study are registered on questionnaire sheets to be analyzed, examined, and confirmed or overturned at the end. Then these data were analyzed by IBM-SPSS Statistics Base 21. A descriptive and quantitative statistical approach was used to analyze the demographic features (ANOVA One-way and Independent Samples T-Test). Besides, the recorded data were analyzed by multiple quantitative indices like relative frequency of citation (RFC), plant part value (PPV), and informant consensus factor (ICF).

2.2.3.1. Frequency (FC) and relative frequency of citation (RFC). Relative frequency of citation is obtained by dividing frequency citation (FC) by a total number of respondents in the study (N). The RFC value for species is based on the citing portion of respondents for every plant. RFC was determined by applying this formula (Tardío & Pardo-de-Santayana, 2008): with ($0 < RFC < 1$).

2.2.3.2. Plant part value (PPV). Plant part value (PPV) was determined applying the following equation(Chaachouay et al., 2019a, 2019b, 2019c, 2019d): Wherever RU is the number of applications described of total parts of the plant and $RU_{plant\ part}$ is the sum of uses reported per part of the plant. The part with the most important PPV is commonly used by the informants.

2.2.3.3. Informant consensus factor (ICF). The ICF reflects the homogeneity of information provided by different informants regarding medicinal species used to treat a category of ailments (Heinrich et al., 1998). Where Nur is the number of use-reports in each disease category and Nt is the number of taxa used. The values for the factor range from 0 to 1.

3. Results

3.1. Demographic characteristics

The indigenous knowledge was obtained from 1000 local people in the study area. Based on socio-demography, the participants were categorized into various groups as given in Table 1. Among the participants, 65.4% were men and the remaining were women 34.6%, with a sex ratio man/woman of 1.89. In terms of age, the age groups of 40–60 were very high compared to other groups (43.6%). Just 30% were more than 60 years old, 22.1% were 20–40 years old, and 4.3% of interviewees were under 20 years old. From the total respondents, 76.5% were married, 15.6% divorced, and 7.9% single. Recognizing the educational class, the preponderance of respondents (51.6%) was illiterate, while 34.1% and 13.6% of respondents attended primary and secondary school, respectively. Only 0.7% of respondents were tended to higher education. Concerning the source of information regarding the therapeutic use of medicinal species, the results showed that 78.5% of interviewed persons refer to the experiences of the other (parents and elderly relatives) for preparing recipes, which confirms the transmission of traditional practices from generation to another. While 20.3% of the population refers to herbalists and 1.2% of users prefer a pharmacist.

Table 1
Summary of demographic data for 1000 informants.

Catrgories	Number of informants	Percent (%)
Gender		
Female	346	34.6
Male	654	65.4
Age ranges		
<20 years	43	4.3
20–40 years	221	22.1
40–60 years	436	43.6
>60 years	300	30
Family status		
Married	765	76.5
Divorced	156	15.6
Single	79	7.9
Educational level		
Illiterate	516	51.6
Primary school	341	34.1
Secondary school	136	13.6
Universitaire	7	0.7
Source of knowledge		
Others experiences	785	78.5
Herbalist	203	20.3
Pharmacist	12	1.2

3.2. Most used botanical families

The current investigation demonstrated that a total of 84 toxic medicinal plants belonging to 67 genera and 30 botanical families were frequently used in the popular local pharmacopoeia of Rif. The taxonomic families with the most represented number of utilized toxic plants were Asteraceae and Fabaceae (9 species each), followed by Apiaceae and Solanaceae (7 species each), Asparagaceae and Amaranthaceae (5 species each), Brassicaceae and Lamiaceae (4 species each), Cucurbitaceae and Euphorbiaceae (3 species each). The other botanical families were served by only 1 or 2 species. These toxic species are presented in alphabetical order. For each plant listed, we give the family, the scientific name, the vernacular name, the used part, the disease treated; the mode of preparation and the route of administration adopted by the indigenous people, as well as the data of FC and RFC are shown in Table 2.

3.3. Relative frequency citation (RFC)

The relative frequency citation index authenticates the frequency of citation of a medicinal plant species used for different human diseases. Results of relative frequency citation (RFC) showed that the highest RFC value was reported for *Rosmarinus officinalis* L. (RFC = 18.9%), followed by *Dittrichia viscosa* (L.) Greuter. (RFC = 16.5%), *Nerium oleander* L. (RFC = 14.6%), *Salvia officinalis* L. (RFC = 11.9%), *Artemisia herba-alba* Asso. (RFC = 9.5%), and *Chenopodium ambrosioides* L. (RFC = 9.3%). The lowest RFC was reported for eleven toxic species (RFC = 0.1%).

3.4. Plant parts used in herbal medicine

Indigenous people in the study area collect diverse plant parts (root, leaf, flower, fruit, bulb, and seed) for the preparation of herbal remedies (Table 2). Based on the plant part value PPV record, leaf (PPV = 0.476) was reported as the principal plant part for herbal medicine followed by seed (PPV = 0.180), root (PPV = 0.108), whole plant (PPV = 0.090),

Table 2
List of poisonous medicinal plants used in the popular pharmacopoeia of the Rif, Northern Morocco.

Family and scientific name	Vernacular name	MP	Poisonous parts and active principles	RA	PG	FC	RFC
Amaranthaceae							
Chenopodium ambrosioides L.	Mkhinza	Decoction	All parts (Ascaridole), (Tampion, 1977)	Oral	RD	93	9.3%
Chenopodium album L.	Labda, Baremren	Infusion	All parts (Nitrates, oxalates), (Bruneton, 1996)	Oral	DSD	07	0.7%
Atriplex halimus L.	Legtef	Infusion	Leaves (Saponines), (Bruneton, 1996)	Oral	GUD	03	0.3%
Chenopodium murale L.	Talekutta	Infusion	All parts (Oxalic acid), (Bruneton, 1996; Hammiche et al., 2013)	Oral	DSD	01	0.1%
Salsola kali L.	El Herd	Infusion	All parts (saponines), (Bellakhdar, 1997)	Oral	DSD	01	0.1%
Apiaceae							
Foeniculum vulgare Mill.	Lbesbas	Decoction	All parts (Flavonoids and saponosides), (Bruneton, 1996)	Oral	DSD	68	6.8%
Pimpinella anisum L.	Habbat Hlawa	Other	Fruit (Flavonoids, glucosides), (Bruneton, 1996)	Oral	GUD	35	3.5%
Carum carvi L.	Karwiya	Infusion	Seeds (Essential Oil), (Charnot and Faure, 1945)	Oral	DSD	26	2.6%
Conium maculatum L.	Choukran	Cataplasm	All parts (Alkaloid, coniine) (Keeler et al., 1978)	Dermal	GUD	13	1.3%
Ferula communis L.	Lkalkha	Decoction	All parts (Prenylated coumarins), (Hammiche et al., 2013)	Oral	MD	04	0.4%
Cuminum cyminum L.	Camoun	Infusion	All parts (Terpenes), (Bruneton, 1996)	Oral	DSD	03	0.3%
Thapsia garganica L.	Deryas	Cataplasm	All parts (Resin), (Hammiche et al., 2013)	Dermal	RD	02	0.2%
Apocynaceae							
Nerium oleander L.	Defla, Alili	Decoction	Leaves (Steroid glycosides: oleandrin, nerioside), (Keeler et al., 1978)	Oral	RD	146	14.6%
Araceae							
Arisarum vulgare O.Targ.Tozz.	Irni	Decoction	All parts (Saponosides), (Bruneton, 1996)	Oral	DD	14	1.4%
Aristolochiaceae							
Aristolochia baetica L.	Berztem	Cataplasm	All parts (Aristolochic acid), (Bruneton, 1996; Hammiche et al., 2013)	Atmospherically	GUD	43	4.3%
Asparagaceae							
Asphodelus microcarpus Salzm. & Viv.	Lberwag, Inghri	Decoction	All parts (Alkaloids, saponosides, tanins), (Hosni et al., 2019)	Oral	ND	36	3.6%
Drimia maritima (L.) Stearn.	Ansal	Decoction	All parts (Heterosides), (Hammiche et al., 2013)	Oral	DSD	04	0.4%
Asparagus officinalis L.	Sakkum, Tazzut	Decoction	All parts (Alkaloids, flavonoids), (Bruneton, 1996)	Oral	DSD	02	0.2%
Asparagus acutifolius L.	Sekkom, Tazzut	Decoction	All parts (Alkaloids, flavonoids), (Bruneton, 1996)	Oral	DSD	01	0.1%
Asparagus densiflora Kunth	Sekkom, Tazzut	Other	All parts (Alkaloids, flavonoids), (Bruneton, 1996)	Oral	DSD	01	0.1%
Asteraceae							
Dittrichia viscosa (L.) Greuter.	Magraman, Terrahla	Other	All parts (Methanolic extracts), (Célia et al. s. d.)	Oral	DD	165	16.5%
Artemisia herba-alba Asso.	Chih, Izri	Decoction	All parts (Terpenes), (Zaim et al., 2012)	Oral	ND	95	9.5%
Anacyclus pyrethrum (L.) Lag.	Tiguentest, Ginass	Infusion	All parts (Ethanolic extract), (Sujith et al., 2012)	Oral	RD	81	8.1%
Silybum marianum (L.) Gaertn.	Tawra	Decoction	All parts (Carvone), (Bruneton, 1996)	Oral	GUD	76	7.6%
Artemisia absinthium L.	Chiba	Decoction	All parts (thuyone), (Charnot and Faure, 1945)	Oral	DSD	75	7.5%
Tanacetum vulgare L.	Lbalssem	Infusion	All parts (Alpha-thuyone), (Bellakhdar, 1997; Bruneton, 1996)	Oral	MD AN, HC	42	4.2%
Lactuca virosa Habl.	Ahchlaf Nssem	Other	All parts (Scopolamine), (Besharat et al., 2009)	Oral	DD	16	1.6%
Atractylis gummifera Salzm. ex L.	Addad	Other	All parts (Glycosides), (Hammiche et al., 2013)	Oral	DD	05	0.5%
Artemisia mesatlantica Maire.	Chih, Izri	Decoction	Leaves (Essential oil), (Bruneton, 1996)	Oral	ND	01	0.1%
Brassicaceae							
Lepidium sativum L.	Habb Rchad	Cooked	Seeds (Flavonoides), (Bellakhdar, 1997; Bruneton, 1996)	Oral	RD	21	2.1%
Brassica oleracea L.	Karnabite	Other	All parts (Alcaloids), (Hammiche et al., 2013)	Oral	MD	09	0.9%
Brassica nigra (L.) K. Koch.	Khrdal, Bohamo	Infusion	Seeds (Glucosinolates), (Bellakhdar, 1997; Bruneton, 1996)	Oral	RD	06	0.6%
Brassica rapa L.	Left Lbeldi	Cooked	All parts (Tannins, saponosides), (Charnot and Faure, 1945; Hammiche et al., 2013)	Oral	RD	06	0.6%
Boraginaceae							
Borago officinalis L.	El Hamhem	Infusion	Leaves (Alcaloids), (Bruneton, 1996; Keeler et al., 1978)	Oral	GUD	02	0.2%
Cannabaceae							
Cannabis sativa L.	Lkif	Cataplasm	All parts (Terpenophenols), (Bruneton, 1996; Hammiche et al., 2013)	Atmospherically	DD	11	1.1%
Cucurbitaceae							
Citrullus colocynthis (L.) Schrad.	Lhdej, Taferzizte	Infusion	Fruits and seeds (Cucurbitacins, glycosids), (Hammiche et al., 2013)	Oral	MD	09	0.9%
Bryonia dioica Jacq.	Aineb Edib	Decoction	All parts (Cucurbitacins, glycosids), (Hammiche et al., 2013)	Oral	DSD	05	0.5%
Ecballium elaterium (L.) A.Rich.	Faggous El Hemar	Other	All parts (Cucurbitacins), (Bruneton, 1996; Hammiche et al., 2013)	Oral	ND	02	0.2%
Dryopteridaceae							
Dryopteris filix-mas (L.) Schott.	Sarkhs Dakar	Decoction	Leaves (Thiaminase, tannins and heteroside), (Charnot and Faure, 1945; Hammiche et al., 2013; Hosni et al., 2019)	Oral	ND	01	0.1%
Euphorbiaceae							

(*continued on next page*)

Table 2 (*continued*)

Family and scientific name	Vernacular name	MP	Poisonous parts and active principles	RA	PG	FC	RFC
Euphorbia falcata L.	Hayat Nofos	Infusion	All parts (Terpenes), (Bruneton, 1996)	Oral	RD	63	6.3%
Ricinus communis L.	Kherouâ, Uwriwra Krank	Infusion	Seed (ricin) (Keeler et al., 1978)	Oral	DD	51	5.1%
Mercurialis annua L.	Hrriyga Lmelsa	Decoction	All parts (Saponines), (Bellakhdar, 1997; Bruneton, 1996; Hammiche et al., 2013)	Oral	GUD	05	0.5%
Fabaceae							
Trigonella foenum-graecum L.	Helba	Cooked	Seed (Alkaloids, canavanine), (Charnot and Faure, 1945; Keeler et al., 1978)	Oral	DSD	54	5.4%
Vicia faba L.	Elfûl, Ibaouen	Cooked	All parts (Alkaloids, canavanine, β-ODAP, wistarine, phasin), (Iqbal, 2016)	Oral	RD	51	5.1%
Retama raetam (Forssk.) Webb.	Rtem	Decoction	All parts (Alkaloids), (Bellakhdar, 1997; El Hamdani et al., 2015)	Oral	ND	41	4.1%
Glycyrrhiza glabra L.	Arq Sûs	Infusion	All pars (Saturated fatty acids), (Nazari et al., 2017)	Oral	DSD	36	3.6%
Retama monosperma (L.) Boiss.	Rtem	Decoction	All parts (Alkaloids), (Bellakhdar, 1997; El Hamdani et al., 2015)	Oral	ND	32	3.2%
Lupinus pilosus L.	Rjel Djaja	Infusion	All parts (Alkaloids) (Keeler et al., 1978)	Oral	MD	07	0.7%
Medicago sativa L.	Fessa	Decoction	Seeds (Terpenes), (Bruneton, 1996; Hammiche et al., 2013)	Oral	DSD	05	0.5%
Lupinus angustifolius L.	Shenqala, Bozghiba	Decoction	Alkaloids (Keeler et al., 1978)	Oral	GUD	01	0.1%
Vicia sativa L.	Guersana	Infusion	All parts (Canavanine), (Enneking, 1994)	Oral	RD	01	0.1%
Lamiaceae							
Rosmarinus officinalis L.	Azir, Yazir	Decoction	All parts (Flavonoids, Triterpenes), (Bruneton, 1996; Miresmailli et al., 2006)	Oral	MD	189	18.9%
Salvia officinalis L.	Salmiya	Decoction	All parts (Flavonoids, Triterpenes), (Halicioglu et al., 2011)	Oral	DSD	119	11.9%
Mentha pulegium L.	Fliyou	Infusion	All parts (Pulegone), (Mozaffari et al., 2013)	Oral	ND	67	6.7%
Origanum majorana L.	Mard'douch	Infusion	All parts (Terpens), (El-Ashmawy et al., 2005)	Oral	DSD	46	4.6%
Linaceae							
Linum usitatissimum L.	Zeri't El Kettan	Cooked	Seeds (Lignans), (Bruneton, 1996; Hammiche et al., 2013; Keeler et al., 1978)	Oral	MD	65	6.5%
Malvaceae							
Malva silvestris L.	Bakkula	Cooked	All parts (Tanins, coumarines), (Bellakhdar, 1997; Bruneton, 1996; Keeler et al., 1978)	Oral	DSD	06	0.6%
Malva hispanica L.	Khobbeyza	Decoction	All parts (Tanins, coumarines), (Bellakhdar, 1997; Bruneton, 1996; Keeler et al., 1978)	Oral	DSD	04	0.4%
Myrtaceae							
Eucalyptus globulus Labill.	Kalitûs	Cataplasm	Leaves (Essential oils), (Negahban and Moharramipour, 2007)	Atmospherically	RD	65	6.5%
Eucalyptus camaldulensis Dehnh.	Kalitûs	Decoction	Leaves (Essential oils), (Negahban and Moharramipour, 2007)	Oral	DSD	05	0.5%
Myristicaceae							
Myristica fragrans Houtt.	Bsibissa	Cooked	Seeds (Myristicin), (Keeler et al., 1978)	Oral	GUD	03	0.3%
Nitrariaceae							
Peganum harmala L.	El Harmel	Cataplasm	All parts (Alcaloids), (BOUZIANE & OULD, 2012)	Dermal	ND	53	5.3%
Papaveraceae							
Papaver rhoeas L.	Bela'man	Infusion	All parts (Alcaloids), (Bruneton, 1996; Charnot and Faure, 1945)	Oral	DD	34	3.4%
Fumaria officinalis L.	Hchicht Essibyan	Decoction	All parts (Alcaloids), (Bruneton, 1996; Charnot and Faure, 1945)	Oral	MD	01	0.1%
Pinaceae							
Cedrus atlantica (Endl.)	Arz El Atlas	Other	Leaves (Essential oil), (Bellakhdar, 1997; Bruneton, 1996)	Oral	DD	45	4.5%
Polygonaceae							
Rumex acetosa L.	Houmida	Infusion	All parts (Terpenoides), (Bruneton, 1996; Hammiche et al., 2013)	Oral	DSD	09	0.9%
Poaceae							
Phragmites communis Trin.	Kseb	Infusion	All parts (Gallic acid), (Bruneton, 1996; Charnot and Faure, 1945)	Oral	DSD	74	7.4%
Festuca arundinacea Schreb.	Aguzmir	Infusion	Seeds (Alcaloide), (Bellakhdar, 1997; Charnot and Faure, 1945)	Oral	DSD	05	0.5%
Cynodon dactylon (L.) Pers.	N'jem	Infusion	All parts (Hydrocyanic acid), (Bruneton, 1996; Charnot and Faure, 1945)	Oral	DSD	02	0.2%
Ranunculaceae							
Nigella sativa L.	Sanûj	Infusion	Seeds (Essential oils), (Bruneton, 1996; Charnot and Faure, 1945)	Oral	RD	78	7.8%
Ranunculus bullatus L.	Wden Elhallouf	Decoction	Leaves (Terpenes), (Bruneton, 1996; Charnot and Faure, 1945)	Oral	RD	02	0.2%
Rutaceae							
Citrus × *aurantium* L.	Larnej	Cooked	Leaves (Essential oils), (Bruneton, 1996; Charnot and Faure, 1945)	Oral	RD	25	2.5%
Ruta montana (L.) L.	Fijel, Iwermi	Decoction	All parts (Coumarins, Alkaloids, Lignans), (Hammiche et al., 2013)	Oral	DSD	12	1.2%
Schisandraceae							
Illicium verum Hook.f.	Badiana	Infusion	All parts (Ketones), (Hammiche et al., 2013; Keeler et al., 1978)	Oral	DSD	04	0.4%
Scrophulariaceae							
Verbascum sinuatum L.	Torah	Infusion	All parts (Saponines), (Bellakhdar, 1997; Bruneton, 1996)	Oral	DSD	01	0.1%
Solanaceae							
Capsicum annuum L.	Tahmira	Cataplasm	All parts (Glycoalcaloides), (Hammiche et al., 2013)	Dermal	DD	87	8.7%
Solanum tuberosum L.	Batâta	Cataplasm	All parts (Glycoalcaloides), (Hammiche et al., 2013)	Atmospherically	ND	78	7.8%
		Other	All parts (Alcaloids), (Bruneton, 1996)	Atmospherically	DD	36	3.6%

(*continued on next page*)

Table 2 (*continued*)

Family and scientific name	Vernacular name	MP	Poisonous parts and active principles	RA	PG	FC	RFC
Mandragora autumnalis Mill.	Bid Al Ghol, Taryâla						
Solanum sodomaeum Dunal.	Tfah Lfar	Cataplasm	All parts (Glycoalcaloides), (Hammiche et al., 2013)	Dermal	RD	07	0.7%
Capsicum frutescens L.	Sudaniya, Flfel Har	Decoction	All parts (Glycoalcaloides), (Hammiche et al., 2013)	Oral	DD	05	0.5%
Datura stramonium L.	Chedak Jmal	Other	All parts (Atropine, related alkaloids) (Keeler et al., 1978)	Oral	ND	02	0.2%
Solanum nigrum L.	Buqnîna	Infusion	All parts (Glycoalcaloides), (Hammiche et al., 2013)	Oral	DSD	01	0.1%
Urticaceae							
Urtica dioica L.	Hriga	Cataplasm	All parts (Flavonoids, Coumarines), (Bruneton, 1996; Charnot and Faure, 1945)	Atmospherically	DSD	41	4.1%
Urtica urens L.	Lhurriga	Decoction	All parts (Flavonoids, Coumarines), (Bruneton, 1996; Charnot and Faure, 1945)	Oral	RD	14	1.4%

DD: Dermatological Diseases, **RA:** Route of administration, **DSD:** Digestive system diseases, **GUD:** Genito-Urinary diseases, **MD:** Metabolic Diseases, **MP:** Mode of preparation, **ND:** Neurological Diseases, **RD:** Respiratory Diseases, **PG:** Pathological Groups.

other combination (PPV = 0.055), and fruit (PPV = 0.047). While flower and bulb constitute PPV = 0.027 and PPV = 0.018, respectively.

3.5. Preparation modes and routes of administration

Indigenous people in the study area used different modes of preparation (Table 2). The result showed that the most common method of preparation was decoction (40.6%), followed by infusion preparation (25.2%), cataplasm (15.4%), other modes (12.1%) of preparation (maceration, raw, and fumigation) and cooked (6.7%). As regards routes of administration, the majority of locally prepared remedies were administered orally (84.8%) followed by atmospherically (12.2%) and dermal (3%).

3.6. Diseases treated and their ICF values

The present study reported a total of 2663 reports of different diseases categorized into 6 categories. In the results, ICF varied from 0.9546 to 0.9786 (Table 3), where the dermatological diseases have elevated ICF value of 0.9786, with 469 use-reports for 11 toxic medicinal plants used followed by metabolic diseases (ICF = 0.9784), respiratory diseases (ICF = 0.9772), neurological diseases (ICF = 0.9754), and genitourinary diseases (ICF = 0.9555). The least ICF was associated with digestive system diseases (ICF = 0.9546).

3.7. Knowledge of poisonous plants

Knowing the poisonous plants will help us avoid sustaining injuries from them. Recognition of poisonous plants will help to minimize the potential for poisoning from poisonous plants. The reason for the therapy use of the natural products is the presence of compounds of diverse biologically active plant constituents or phytochemicals (secondary metabolites) such as saponins, terpenes, quinones, flavonoids, alkaloids, tannins, terpenoids, and so on that may act independently, additively or in synergy to show an effect which may be helpful or harmful to health. Some of these plants have been assigned as poisonous plants because of their effects on impacting biological functions in other organisms which are harmful (Mensah et al., 2019). The study reveals that 21% of interviewed know about plant toxicity, especially elder people. On the other side, 79% of the local population ignores any information on toxic plants and their dangers on health.

Table 3
ICF values by categories for treating human diseases in the Rif region.

Diseases treated	Nt	Nur	ICF
Dermatological diseases	11	469	0.9786
Metabolic diseases	8	326	0.9784
Respiratory diseases	16	661	0.9772
Neurological diseases	11	408	0.9754
Genitourinary diseases	9	181	0.9555
Digestive system diseases	29	618	0.9546

3.8. Care results

Questions addressed to the informants were mainly focused on the toxic symptoms of plant ingested, toxic parts, the manner of administration and toxicity. On improving patient health, 67% of indigenous people interviewed believe that medicinal plants allow provide a cure for diseases. While 28% consider that the use of medicinal plants can just be contributing to improvement the health status. However 5% assume that treatment by plants creates undesirable side effects. According to field observations in the Rif, prolonged ingestion of large single doses of these plants induces a chronic intoxication in humans characterized by skin irritation, ulcers, arthritis, gastric inflammation, abdominal disturbances, abortion, hysteria, mannia, epilepsy, asthma, bronchitis, diarrhea, general fatigue, dysentery, dizziness, anoxia and spasm.

4. Discussion

A total of 84 toxic plants belonging to 67 genera and 30 floral families were documented from the study area as having rich healing uses. The Asteraceae and Fabaceae families were represented by the largest number of species with 9 poisonous species each (Bellakhdar, 1997c; Bruneton, 1996c; Charnot and Faure, 1945b; Mensah et al., 2019b), followed by Apiaceae and Solanaceae with 7 poisonous species each (Bellakhdar, 1997 c; Mensah et al., 2019; Mounanga et al., 2015; Rhalem et al., 2009b; Zekkour, 2008c). These results are in general accordance with some ethnobotanical studies which indicated that the most prominent families were Asteraceae and Fabaceae (Amiri et al., 2014; Chaachouay et al., 2019a, 2019b, 2019c, 2019d; Cheikhyoussef et al., 2011; Maneenoon et al., 2015). The most important total of medicinal plants from these families may be due to their extensive distribution, richness, abundance, and a wide variety of phytochemical compounds in the species taxa belonging to this family in the Rif's area. Toxicological investigations on these plant families could contribute insights into their rich phytoconstituents and images of the pharmacological effects of their active composites (Ramana, 2008).

RFC is applied to determine the most frequently used plant species used for different human diseases in the Rif. In the present study, the toxic plants with a high degree of RFC were *Rosmarinus officinalis* L. (18.9%), followed by *Dittrichia viscosa* (L.) Greuter. (16.5%), *Nerium oleander* L. (14.6%), *Salvia officinalis* L. (11.9%), *Artemisia herba-alba* Asso. (9.5%). The results reveal that more autochthonous people have a better understanding of medicinal plantsŏ as we find that the population is aware of the toxicity of certain parts of the plant which they avoid. Therefore, plant species that were not previously studied but have a high

RFC should be further evaluated using toxicological and phytochemical techniques for drug discovery.

In the present investigation, several plant parts were used as different remedies by local people of the Rif. Results revealed that greater proportion was leaf (PPV = 0.476) followed by seed (PPV = 0.180), root (PPV = 0.108). Our finding on the proportions of different plant parts used in the Rif coincides with most of the other ethnobotanical investigations that have registered the predominance of leaves as being employed in the preparation of herbal drugs (Benarba et al., 2014; Chaachouay et al., 2019a, 2019b, 2019c, 2019d; Islam et al., 2014; Mussarat et al., 2014; Noman et al., 2013). The purpose of why leaves were frequently used could be that they are simply available and are active in photosynthesis and production of metabolites. Additionally, the collection of leaves has a less detrimental impact on plants compared to the harvesting of roots, fruit, and stem especially where there are no sustainable harvesting procedures in place (Asase et al., 2010).

The ICF indicates the consensus between plant species and informants concerning to the treatment of ailments. The results of the informant consensus factor calculation show that the value ranges from 0.9546 to 0.9786. Dermatological diseases have a high ICF value of 0.9786, with 469 use-reports for 11 toxic plant species. It signifies the best consensus between plant species and treated dermatological diseases because local people interviewed used precise plant species commonly for dermatological diseases. The second highest ICF was found for metabolic diseases (ICF = 0.9784), followed by respiratory diseases (ICF = 0.9772). High ICF is correlated to species that could be efficient in treating a particular ailment (Uddin and Hassan, 2014). Consequently, species with high ICF are to be prioritized for further toxicological and pharmacological studies.

In herbal medicine, there are several modes of preparing plants, depending on the use you want to make of them. The results showed that the majority of remedies were prepared from decoction (40.6%), followed by infusion (25.2%), cataplasm (15.4%), other modes (12.1%), and cooked (6.7%). These results are in general accord with previous ethnobotanical inventories which designated that the most important mode of preparation was decoction (Ahmad et al., 2014; Benkhnigue et al., 2010; Chaachouay et al., 2019a, 2019b, 2019c, 2019d; Shinwari et al., 2017). Furthermore, these results explain that the indigenous people in the Rif region believe in decoction mode and found it suitable for heating the body and decontaminating the plants. Indeed the decoction allows collect the most for the active ingredient and attenuates or cancels the toxic effect of certain recipes (Chaachouay et al., 2019a, 2019b, 2019c, 2019d; Salhi et al., 2010). The routes administration in this study changes with the type of ailment treated and the actual sites of the diseases. The result revealed the most route of application for herbal therapeutics was oral (84.8%). Also, the oral administration is a favored route all over the globe (Andrade et al., 2017; Chaachouay et al., 2019a, 2019b, 2019c, 2019d; Kichu et al., 2015; Ullah et al., 2013). Nevertheless, the recommendation of medicinal plants, essentially based on oral administration represents a real health danger.

Botanical misidentification or mislabeling of plant material can play a role for toxic reactions in humans. In Morocco, a descriptive retrospective study was conducted on all poisoning cases reported between 1981 and 2004 at the Moroccan Poison Control and Pharmacovigilance Center (MPCPC). During this period, 240 people were hospitalized for *Atractylis gummifera* Salzm. ex L. poisoning, 72% of whom were children under the age of 16 (Hami et al., 2011). *Peganum harmala* L. poisoning is not uncommon: it represents 4.6% of all herbal poisonings received at the country's Poison Control Center (Rhalem et al., 2010).

It is not only botanical misidentification or contamination with toxic and undeclared constituents. Unprofessional processing, which differs from safe traditional preparation represents another source for herbal poisoning. Toxicity of toxic medicinal plants may be related to the mixtures of active compounds that they contain; their interactions with other herbs and drugs, contaminants, adulterants; or their inherent toxicity (Saad et al., 2006). The concentration of active ingredients and other chemicals in plants varies by the part of the plant harvested and sold; the maturity of the plant at the time of harvest; the time of year during harvest; geography and soil conditions; soil composition and its contaminants; and year-to-year variations in soil acidity, water, weather conditions and other growth factors (Ralphs et al., 1988; Saad et al., 2006).

For all plant species, many phytotoxins were identified and classified into the different plant secondary metabolite classes, as indicated in Table 2. The highest number of toxins is found for alkaloids. Alkaloids are one of the main components that can cause poisoning. Plant secondary metabolite classes with intermediate phytotoxin numbers are the saponins, steroids, phenylpropanoids, and polyketides. The diagnosis of plant poisonings in humans is not always simple, and depends on a good case history and an evaluation of pathological lesions and clinical signs, as well as confirmatory laboratory tests where these exist. Treatment is not always possible or successful, and prevention remains the most important way to protect humans.

5. Conclusions

In total, 84 poisonous medicinal plants belonging to 67 genera and 30 families were reported to be used by indigenous people from Northern Morocco. This study demonstrates that the practice of herbal medicine in the Rif region is increasing incredibly; our informants blindly trust this medicine without taking into account the danger of these plants on their health and this is due to the know-how acquired, the population (older) has learned relatively to recognize the dose and the part which brings the least toxicity (local culture to save). Medicinal plants, like medicines, must obey strict standard rules that only the herbal medicine professional can meet. Therefore, attention should be employed when using these plants, especially medicinal purposes. It is important to obtain information on these medicinal plant-based remedies prepared and prescribed by therapeutics, especially in terms of toxicity, composition, specific effectiveness of illness, and to encourage practitioners of this herbal medicine on the protection and safeguard of patients. This necessarily means regulating the profession in our country. We believe that any poisonous plant or ingredients taken from toxic plants should be tested before being used as a remedy. Hence, various advanced cell biological, biochemical, molecular biological and *in vitro* cell culture techniques should be applied with different medicinal herbs in order to test their safety before testing their efficacy.

Ethical approval and consent to participate

Consent for this research was granted by the Committee for ethical research of the Ibn Tofail University, Kenitra. Interviewees were informed that the intentions of the research were not for commercial purposes or other interests but academic reasons. Informants provided verbal informed consent to share in this study; they were free to withdraw their knowledge at any point in time.

Consent for publication

Not applicable.

Availability of supporting data

All data gathered and analyzed in this study are included in the article and joined in the form of 'Appendices' as supplementary data. Plant species are stored in Ibn Tofail University, Kenitra, Morocco.

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Authors' contributions

NC: Carried out field research in the Rif, compiled the literature sources, data analysis, Realization manuscript and evaluation, interpretation, and wrote the manuscript. **OB:** Helped in data and made a substantial contribution to data analysis. **AD:** Performed data analysis and drafted the manuscript. **LZ:** Designed the research and identification of plant species. All authors see and affirmed the final document.

Declaration of competing interest

We certify that there is no conflict of interest with any financial organization regarding the manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.toxicon.2020.10.028.

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